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THE CHEMOTHERAPY OF GONORRHŒA FAILURES. THEIR CAUSE AND PREVENTION *

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I AM going to put before you a few facts and figures to indicate that we have at last a drug that is all powerful in combating and curing gonorrhœa in the female. This infection, which has been the despair of all venerealogists and gynæcologists for years, formerly only yielded to long and meticulous treatment, and even when the patient was discharged after such lengthy treatment and repeated tests as probably cured, one feared to hear later of a relapse.

Since 1914, when I first started treating this disease at the London Lock Hospital, I have been convinced that some day a drug affecting the general system would be found to cure gonorrhœa. It seemed to me to be irrational that treating a local condition merely by local applications could effect a certain cure of a disease which had so many ramifications. Over 20 years later my hopes have materialised and now gonorrhœa is no longer the dreaded disease that it was. In women it was, in my former opinion, far worse than syphilis.

In October, 1936, the treatment of gonorrhœa by chemotherapy was adopted in the Female Department for Venereal Diseases at Guy's Hospital; I believe that Guy's was the pioneer in this method of treatment. We tried Proseptasine, Sulphanilamide and finally M. & B. 693. I want to impress upon you the revolution that the latter drug has effected in the treatment of gonorrhœa in women. Our old treatment of gonorrhœa consisted of meticulous care in swabbing the vulva and vagina, and if necessary syringing the ducts daily with whatever disinfectant happened to be on trial; also treatment by pessaries, suppositories and vaccines, and in severe cases rest in bed. We employed douching only when the

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Fallopian tubes were infected, as I had a very firm impression that indiscriminate douching tended to cause salpingitis. This treatment had to be maintained for months, indeed sometimes for years.

Now M. & B. 693, three grammes per day, is given in one gramme doses for a period of one week. No local treatment is given except for the occasional insertion of a vaginal speculum and cleaning out with distilled water. This enables us to watch progress and to take tests; incidentally, it has a good psychological effect on the patient; she feels that something is being done for the affected part. Such treatment with M. & B. 693 brings about what I firmly believe to be a true and lasting cure. I am stressing our omission of local treatment as I believe it is the practice at some clinics to continue such treatment during the period of drug administration.

I now propose to give my results as regards failures from the three compounds used, namely, Proseptasine, Sulphanilamide and M. & B. 693. Before giving these figures I wish to emphasise that there is a real difficulty in diagnosing which is a relapse and which a reinfection. It is not easy to get the whole truth from a female patient suffering from venereal disease; she does not like to confess that she has failed in strict observance of the instructions that she has received. For instance, one patient developed rectal gonorrhœa after a course of treatment and many negative tests; it was only after a very private talk that I elicited that a risk of rectal gonorrhœal infection had been a possibility. This case I counted as a reinfection.

I have, however, obtained the following figures from my own cases which I believe to be strictly accurate. Of the cases treated with Proseptasine, 16 per cent. definitely relapsed. Of these relapses two-thirds were in a chronic condition when chemotherapy began and one-third were acute. The average total amount of the compound found to be necessary for a satisfactory result was 70 grammes over a period of four weeks.

Of those receiving Sulphanilamide, 20 per cent. relapsed. The infection had been chronic at the commencement of treatment with chemotherapy in 60 per cent. of the cases and acute in 40 per cent. The average total amount of Sulphanilamide given was 48 grammes over a period of $4\frac{1}{2}$ weeks.

Of the first 100 consecutive cases treated with M. & B. 693 only four relapsed. In two of these relapsed cases treatment had been started in the chronic stage and in two in the acute stage. The average total amount given was 27 grammes in two weeks or less. The amount finally found to be sufficient was 21 grammes over a period of one week.

The difference in the results of the three drugs employed was so overwhelmingly in favour of M. & B. 693 that we now use this compound only and I am therefore limiting my remarks to the four failures.

Three of the four relapsing cases had received inadequate treatment on account of intolerance.

The fourth, an acute infection, had received high dosage—36 grammes—but six weeks later gonococci were found in films from the urethra and cervix. She has now been watched for 14 months after a second course of 24 grammes of M. & B. 693 and her condition, and that of her husband, remains satisfactory. This case has been classified as a relapse, although I have my doubts.

Of the three patients who received inadequate treatment the first was a pregnant woman with chronic gonorrhœa who was transferred to another hospital because of the pregnancy. She developed a toxic rash after eight grammes of M. & B. 693, which was then discontinued. Gonococci were found on culture at another hospital four days after the cessation of treatment, but further details are unknown.

The second patient, whose infection was acute, also received inadequate dosage—14 grammes—on account of a toxic rash and relapsed three weeks later. After a second course of M. & B. 693—35 grammes—all tests were negative during the subsequent six months.

The third patient, a married woman with a chronic infection previously resistant to Sulphanilamide, showed considerable intolerance to M. & B. 693, namely, headaches, general malaise and fainting attacks, and therefore had a small course—14 grammes. She relapsed nine days later. A second course of 10½ grammes also reduced for the same reason resulted in a cure. She has remained negative for 20 months and her husband also remains well.

As regards the dosage, I consider that 21 grammes is an ideal amount ; I have, however, seen cases responding

to less, but for safety, in view of the relapses, we try to give not less than 21 grammes. Usually, negative tests are obtained as soon as 48 hours after the commencement of treatment. In comparing the three compounds it has been noticed that more cases were intolerant to M. & B. 693 than to Sulphanilamide or Proseptasine. Intolerance was usually very slight and in such cases we no longer omit chemotherapy but continue with the one week's course of 21 grammes. In no case has it been noticed that a reaction interfered with the beneficial action of the drug when the course was maintained.

Our tests for cure after cessation of treatment are examination of films and cultures taken at first weekly, then every fortnight, and then monthly after provocative treatment. Finally, after six months' observation a complement fixation test is done, as also cultures and films after a provocative vaccine.

Realising the difficulty in proving a cure in women, I recently followed up all married patients who were cohabiting with their husbands. It seemed to me that if these women had not relapsed the probability of cure was more certain. Of the first 100 cases 53 per cent. were married women and 56 per cent. of these had husbands treated at Guy's Hospital. Eighty per cent. of these women were negative on tests and on clinical examination. The condition of their husbands was said to be satisfactory. The remaining 20 per cent. had ceased to attend before the completion of their six months' tests, but I feel certain that they would have returned quickly with complaints from themselves or their husbands if all had not been satisfactory.

Of all cases under treatment with M. & B. 693, only 8 per cent. attended for less than two months' observation; 45 per cent. had from six to 22 months' observation and have been discharged, and the remainder are still under observation. The time of relapse after treatment with M. & B. 693 has varied from four to 45 days. The longest period before relapse in any patient was four months, in a woman treated with Sulphanilamide.

I have counted as acute those cases which had a history of a risk of infection not longer than one month. Women so often have a sub-acute condition from the start that it is difficult to classify them as acute or chronic in any other manner.

In no case has a tubal infection occurred during or after treatment except in one case which I have classed as a reinfection following a dilatation and curetting by a gynæcologist who had no knowledge of the latent gonococcal condition.

To summarise, I consider that M. & B. 693 surpasses other chemotherapeutic agents in the treatment of gonorrhœa in women because of the smaller dosage required, the shorter period of treatment and the fewer relapses. I consider that the reactions which undoubtedly occur during even a short course of treatment do not necessitate the omission of the drug unless marked toxicity is encountered. I believe that our low percentage of failures may be due firstly to the dosage employed and secondly to the absolutely conservative local treatment given. Surely this conservative treatment leaves the mucous membrane in a more favourable state for the drug to do its work on than when the local tissues are affected by antiseptics. I consider that the absence of any gonococcal complications during and after chemotherapy is most striking. This fact alone has robbed gonorrhœa of its terror and preserves the child-bearing capacity of the patient, a matter of great importance at the present time.

In conclusion I thank my assistant, Dr. Bolton, and my Almoner, Miss Manwaring, for their very valuable help.